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DOI:

[10.1002/uog.20132](https://doi.org/10.1002/uog.20132)

*Document Version*

Peer reviewed version

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*Citation for published version (APA):*

Webster, L. M., Bramham, K., Seed, P. T., Homsy, M., Widdows, K., Webb, A. J., Nelson-Piercy, C., Magee, L., Thilaganathan, B., Myers, J. E., & Chappell, L. C. (2019). The impact of ethnicity on adverse perinatal outcome in women with chronic hypertension: a cohort study. *Ultrasound in Obstetrics and Gynecology*, 54(1), 72-78. <https://doi.org/10.1002/uog.20132>

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**The impact of ethnicity on adverse perinatal outcome in women with chronic hypertension:  
a cohort study**

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**Running Head:** Ethnicity and chronic hypertension in pregnancy

**Keywords:** pregnancy, chronic hypertension, ethnicity, stillbirth, fetal growth restriction, prematurity

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/uog.20132

**ABSTRACT**

**Objectives:** This study aimed to assess the impact of maternal ethnicity on the risk of adverse perinatal outcome in pregnant women with chronic hypertension.

**Methods:** Demographic and delivery data of women with chronic hypertension and singleton pregnancies from three obstetric units (2000 to 2014) were collated. Multivariable logistic regression models were used to calculate risk ratios (RR) by ethnic group for adverse perinatal outcome in women with chronic hypertension adjusted for other maternal characteristics. The impact of maternal ethnicity on birthweight centile calculation was investigated by comparing customised birthweight centile (GROW) to birthweight centile calculator that does not adjust for maternal ethnicity (Intergrowth 21<sup>st</sup>).

**Results:** The cohort included 4045 women (4481 pregnancies) with chronic hypertension. Women of White ethnicity accounted for 47% (n=2122) of the cohort; 36% were Black (n=1601) and 8.5% Asian (n=379). The overall incidence of stillbirth was 1.6%, preterm birth <37 weeks 16%, and fetal growth restriction (birthweight <3<sup>rd</sup> centile) 11%. Black women, compared to White women, had the highest risk for all adverse perinatal outcomes: stillbirth 3.1% versus 0.6% (adjusted RR 5.56; 95% CI 2.79 to 11.09), preterm birth <37 weeks 21% versus 11% (aRR 1.70; 95% CI 1.43 to 2.01), birthweight <3<sup>rd</sup> centile 16% versus 7.4% (aRR 2.07; 95% CI 1.71 to 2.51). Asian women, compared to White women, were also at increased risk of adverse perinatal outcomes: stillbirth 1.6% versus 0.6% (aRR 3.03; 95% CI 1.11 to 8.28), preterm birth <37 weeks 20% versus 11% (aRR 1.86; 95% CI 1.44 to 2.40) and birthweight <3<sup>rd</sup> centile 12% versus 7.4% (aRR 1.69; 95% CI 1.24 to 2.30).

**Conclusions:** Black ethnicity (compared to White) is associated with the greatest risk of adverse perinatal outcome in women with chronic hypertension even after adjusting for other maternal characteristics. Women of Asian ethnicity are also at increased risk, but to a lesser extent.

**Health Regulation Authority Approval: 17/HRA/0021**

## INTRODUCTION

Ethnic variation in the incidence of adverse maternal and perinatal outcomes has been reported,<sup>1-4</sup> with women of Black ethnicity being at greater risk of hypertensive disorders of pregnancy compared to White<sup>1,5</sup> as well as other pregnancy-related morbidity and mortality.<sup>3,6</sup> Some postulate that these differences relate predominantly to social deprivation and restricted access to healthcare,<sup>2,7</sup> but given the ethnic variation in pathophysiology observed in conditions such as hypertension outside pregnancy, the mechanisms underpinning these differences in pregnancy warrant further investigation.<sup>8,9</sup>

Chronic hypertension complicates around 3% of pregnancies and is rising in incidence due to increasing maternal age and the global obesity epidemic.<sup>10-14</sup> Superimposed pre-eclampsia, stillbirth, fetal growth restriction, and preterm birth all occur more frequently in pregnancies complicated by chronic hypertension, compared with normotensive pregnancies.<sup>11, 15-18</sup>

Previous population studies have found that young and middle-aged women of Black ethnicity demonstrate a steeper age-gradient in prevalence of chronic hypertension than those of White ethnicity and men of Black ethnicity.<sup>8</sup> Outside pregnancy, ethnic origin is considered when prescribing antihypertensive treatment due to variation in drug response;<sup>19</sup> the potential benefits of tailoring antihypertensive treatment in pregnancy is yet to be elucidated.

Data from contemporaneous cohorts of women with chronic hypertension in pregnancy investigating the relationship between ethnicity and the incidence of adverse perinatal outcome are lacking and could inform research prioritisation, surveillance pathways and stratified treatment options. The objectives of this large multicentre cohort study were to assess the impact of ethnicity on the risk of adverse perinatal outcome in pregnancy complicated by chronic hypertension amongst a population with access to free healthcare.

## METHODS

The cohort was collated from three obstetric units in the UK: Guy's and St Thomas' National Health Service (NHS) Foundation Trust (London), St George's University Hospitals NHS Foundation Trust (London), and Central Manchester University Hospitals NHS Foundation Trust (Manchester). All deliveries after 20 weeks' gestation recorded on maternity databases between 2000 and 2014 with maternal history of chronic hypertension (diagnosed outside of pregnancy) or a documented blood pressure greater than or equal to 140 mmHg systolic and/or 90 mmHg diastolic recorded before 20 weeks' gestation (as per the International Society for the Study of Hypertension in Pregnancy classification)<sup>20</sup> were extracted for analysis. Multifetal pregnancies were then excluded from the cohort due to a risk of confounding perinatal outcomes.<sup>21</sup> Demographic and delivery data were recorded for all the remaining singleton pregnancies complicated by chronic hypertension. Only pregnancies with a complete baseline demographic dataset (comprising maternal age, body mass index (BMI), parity, smoking, ethnicity, and deprivation index) were included in the analysis. The size of the study was dictated by the earliest year maternal demographic and delivery data were recorded electronically at each centre.

Ethnicity (as recorded at antenatal booking) was assigned using four ethnic groups, White, Black, Asian, and Other, based on the grouping used by the UK Office for National Statistics.<sup>22</sup> For example women of European origin were assigned to the White ethnic group, women of West African or Caribbean origin were assigned to the Black group, and women of Indian, Pakistani or Bangladeshi origin were assigned to the Asian group. Women of mixed ethnic origin were included in the group that they shared heritage with in the following order of priority: Black, Asian, White and Other. Socioeconomic status was classified using data from the 2010 UK census (updated in 2015) regarding deprivation in seven domains: Income, Employment, Health, Education, Housing and Services, Crime, and the Living Environment.

Women were linked to one of 32,844 census areas using their full 8-character postcode; participants were then categorised into the five groups with one being the least deprived and five being the most deprived.<sup>23</sup> Where the participant had no fixed abode they were included in deprivation index group five.

Birthweight centiles were calculated using birthweight centile charts (Gestation Related Optimal Weight (version 6.7.5.1 2014) and Intergrowth-21<sup>st</sup> (<http://intergrowth21.ndog.ox.ac.uk/>)).<sup>24, 25</sup> The GROW customised birthweight centiles adjust for maternal height, maternal weight, maternal ethnicity, parity, gestation at delivery, infant sex and infant birthweight in its calculation.<sup>24</sup> The Intergrowth-21<sup>st</sup> birthweight centiles adjust for gestation at delivery, infant sex and infant birthweight.<sup>25</sup> Infants were then categorised into those with a birthweight less than the 10<sup>th</sup> centile and less than the 3<sup>rd</sup> centile (the latter group characterised as fetal growth restriction (FGR) by a recent Delphi consensus<sup>26</sup>). GROW birthweight centiles<sup>24</sup> were used in the primary analysis and Intergrowth-21<sup>st</sup><sup>25</sup> for subsequent comparison. Preterm births (spontaneous and iatrogenic) were categorised as those born before 37 weeks' gestation and 34 weeks' gestation. Stillbirths were defined as infants born without signs of life after 20 weeks' gestation. Neonatal unit admission included infants requiring neonatal intensive care unit and/or special care baby unit admission.

## Statistical Analysis

Means (SD) or medians (IQR) were calculated for continuous variables and numbers with percentages were calculated for categorical data. Within the cohort of pregnancies complicated by chronic hypertension, unadjusted risk ratios and associated 95% CIs were calculated by generalised linear models using the statistical package Stata (version 14.1) for baseline demographic factors and subsequent perinatal outcomes (including stillbirth, preterm birth, neonatal unit admission, birthweight <10th and <3rd centile). Adjusted risk ratios were then calculated using a multivariable regression model comparing ethnicity with other demographic factors that could be explanatory or confounding in association with adverse perinatal outcome: deprivation index, maternal age, parity, BMI, smoking history, and year of delivery. Allowance was made for women having more than one pregnancy within the cohort duration by adjusting the standard errors for clustering by hospital identification number. The validity of the model was confirmed by repeating the multivariable regression only including the significant risk factors for each perinatal outcome. Further associations of maternal characteristics and adverse outcome were explored via chi-squared test or linear regression models. Investigation of possible confounding included assessing the impact of centre of delivery on each perinatal outcome.

The study was registered with the Health Regulation Authority (17/HRA/0021) and reported in line with STROBE guidance for observational studies.<sup>27</sup>

## RESULTS

Data from 4481 singleton pregnancies in 4045 women with chronic hypertension between 2000 and 2014 were included in the analysis. The distribution of ethnicity was 47% (n=2122) White, 36% Black (n=1601), 8.5% Asian (n=379), and 8.5% Other (n=379). The flow diagram of participants is shown in Figure 1. Only pregnancies with all demographic characteristics required for the multivariate regression model were included in the final analysis (86% of singleton pregnancies identified). The most common missing data point was BMI accounting for 13% of pregnancies excluded from the analysis with the majority of these in the earliest years of the dataset. Sixteen postcodes could not be linked to deprivation index as they were incorrectly recorded in the source data; these participants were also excluded from the analysis. Thirteen women had no fixed abode and were included in deprivation index group five. The cohort included 2016 (45%) pregnancies from Guy's and St Thomas' NHS Foundation Trust (London), 2029 (45%) from St George's University Hospitals NHS Foundation Trust (London), and 436 (10%) from Central Manchester University Hospitals NHS Foundation Trust (Manchester). There were a greater number of pregnancies included in the cohort from 2010 onwards as maternity records from Central Manchester University Hospitals NHS Foundation Trust were not available before this date (Table 1).

The proportion of women in this cohort requiring caesarean section was 39% and maternal high dependency unit care was needed for 11%. The incidence of stillbirth was 1.6%, preterm birth before 37 weeks' gestation 16%, birthweight below the 3<sup>rd</sup> centile 11% and neonatal unit admission was required for 9.2% of infants. Maternal and perinatal outcomes for the whole cohort and for each ethnic group are presented in Table 2.



Multivariable regression model analysis comparing ethnicity to other risk factors contributing to adverse perinatal outcome

Using stillbirth as an important perinatal endpoint, the impact of ethnicity and other maternal characteristics was assessed in a multivariable regression model. The only maternal characteristics remaining significant in the adjusted model were Black and Asian ethnicity. Black women had a risk ratio of 5.56 (95% CI 2.79 to 11.09) of having a stillbirth compared to White women, and Asian women had risk ratio of 3.03 (95% CI 1.11 to 8.28) compared to White women (Table S1).

When the risks were calculated for birthweight <3rd centile, an increased risk was seen in women of Black (RR 2.07; 95% CI 1.71 to 2.51), Asian (RR 1.69; 95% CI 1.24 to 2.30) or Other ethnicity (RR 1.70, 95% CI 1.26 to 2.31) (compared to White women), women aged 40 years or older (RR 1.53; 95% CI 1.09 to 2.16) (compared to women aged <40 years), and women who smoked (RR 1.53; 95% CI 1.15 to 2.04) (compared to non-smokers) (Table S2). Baseline characteristics significantly increasing the risk of birthweight <10th centile in the adjusted model included Black ethnicity (RR 1.64; 95% CI 1.45 to 1.87), being aged 40 years or older (RR 1.34; 95% CI 1.06 to 1.69), nulliparity (RR 1.16; 95% CI 1.03 to 1.30), smoking (RR 1.52; 95% CI 1.28 to 1.81), and living in an area of greatest deprivation (RR 1.20; 95% CI 1.04 to 1.38) (Table S3).

Factors increasing the risk of preterm birth before 37 weeks' gestation included: Black or Asian ethnicity (RR 1.70; 95% CI 1.43 to 2.01 and RR 1.82; 95% CI 1.41 to 2.35 respectively), being aged 40 years or older (RR 1.52; 95% CI 1.13 to 2.05), nulliparity (RR 1.17; 95% CI 1.01 to 1.35), and living in an area of greatest deprivation (RR 1.42; 95% CI 1.18 to 1.70) (Table S4). When the analysis was repeated assessing the risk of preterm birth before 34 weeks' gestation, only women of Black (RR 2.69; 95% CI 2.03 to 3.55), Asian (RR 2.48; 95% CI 1.69 to 3.66) and Other

ethnic groups (RR 1.69; 95% CI 1.07 to 2.68), and women living in the most deprived areas (RR 1.39; 95% CI 1.05 to 1.86) were at significantly increased risk (Table S5). In this cohort, where 15.6% of women delivered preterm, 3.2% followed spontaneous labour whilst 12.4% were iatrogenic. No ethnic difference was seen amongst the spontaneous preterm births, but the proportion of Black versus White women giving birth before 37 weeks' gestation through iatrogenic delivery was 17% versus 7.9% ( $p < 0.0001$ ).

Neonatal unit admission was associated with Black, Asian and Other ethnicity compared to White (RR 1.55; 95% CI 1.25 to 1.93, RR 1.58; 95% CI 1.12 to 2.23, and RR 1.46; 95% CI 1.06 to 2.04 respectively), and nulliparity compared to multiparity (RR 1.32; 95% CI 1.08 to 1.61) (Table S6). Year of delivery also affected the risk of neonatal unit admission with babies born between 2000-2004 and 2005-2009 at greater risk than those born between 2010-2014 (RR 1.35; 95% CI 1.05 to 1.74, and RR 1.30; 95% CI 1.06 to 1.60 respectively).

The regression model for each perinatal outcome was repeated including only the data from women who delivered their babies in the last five years of the study as a sensitivity analysis. This ensured that all centres were included for the same time period. The characteristics associated with the greatest increased risk of adverse outcome remained significant. Non-White ethnicity, living in an area of greater deprivation, smoking and primiparity were all associated with and increased risk of adverse outcome in this model (Table S7).

A summary of all the significant adjusted risk ratios and related confidence intervals for the maternal characteristics associated with adverse perinatal outcome in women with chronic hypertension was collated (Table 3).

Further investigation into potential aetiology underpinning disparity in outcome within the cohort of pregnancies complicated by chronic hypertension

Investigation of a surrogate for severity of maternal disease was conducted by comparing the proportion of mothers admitted to the high dependency unit or intensive care unit after birth. Black mothers versus White mothers were more likely to require high-level care after birth, 14% versus 8.2% (odds ratio 1.83; 95% CI 1.46-2.29).

Of stillborn babies, 77% had a birthweight <10<sup>th</sup> centile and 63% had a birthweight <3<sup>rd</sup> centile. Most stillbirths occurred before 37 weeks' gestation (93%). No impact of ethnicity on the proportion of stillbirths with birthweight <10<sup>th</sup> centile or the gestation at delivery was found. Within the entire cohort, the proportion of neonates with birthweight <3<sup>rd</sup> centile was higher amongst those born preterm (54% of births before 34 weeks' gestation and 19% of births 34 to 37 weeks' gestation) compared to 6.9% of births from 37 weeks' gestation (Figure S1). Just over half the infants requiring neonatal admission had birthweights below the 10<sup>th</sup> centile and 40% of infants requiring neonatal unit admission had birthweight <3<sup>rd</sup> centile.

Further investigation of the importance of ethnicity within birthweight centile calculation was assessed by comparing the Intergrowth-21<sup>st</sup> birthweight centiles, which do not include an adjustment for maternal ethnicity, with the GROW birthweight centiles.<sup>24, 25</sup> The proportion of infants classed as <3<sup>rd</sup> birthweight centile was 11% using the GROW versus 5.1% using Intergrowth-21<sup>st</sup> birthweight centiles; those with birthweight <10<sup>th</sup> centile were 23% versus 13% respectively. No infants classed as birthweight <3<sup>rd</sup> centile by Intergrowth-21<sup>st</sup> but not by GROW were admitted to the neonatal care unit; however, 47 infants (12%) requiring neonatal unit admission were classed as birthweight <3<sup>rd</sup> centile by GROW but birthweight >10<sup>th</sup> by Intergrowth-21<sup>st</sup>. The sensitivity and specificity for infants requiring neonatal unit admission were 40% and 93% for those with birthweight <3<sup>rd</sup> centile calculated using GROW, compared to 16% and 96% respectively for those with birthweight <3<sup>rd</sup> centile calculated using Intergrowth-21<sup>st</sup>.

## DISCUSSION

### Main Findings

This large contemporary cohort study of women with chronic hypertension in pregnancy demonstrates that non-White ethnicity (especially Black) is associated with an increased risk of adverse maternal and perinatal outcome. Other maternal characteristics associated with adverse perinatal outcome have also been identified and are consistent with findings of previous studies;<sup>28, 29</sup> advanced maternal age, smoking status, primiparity and deprivation all impact perinatal complications to differing extents.

It is striking that Black ethnicity was consistently associated with the highest increased risk for all adverse outcomes compared with other baseline characteristics in women with chronic hypertension in pregnancy, even after controlling for deprivation, maternal age, BMI, parity, year of delivery, and smoking. The explanation for this is likely to be multifactorial with biological and non-biological factors contributing. Women with chronic hypertension who were of Black (versus White) ethnicity had a more than a five-fold increase in stillbirth risk. A disparity in incidence of stillbirth in women born in African/Caribbean countries (0.7%) compared to women born in the UK (0.5%) is reported by the Office for National Statistics,<sup>30</sup> but these data suggest that the disparity between ethnicities among women with chronic hypertension is much greater. In this cohort, there was greater sensitivity (40% versus 16%) for infants needing neonatal unit admission identified as <3<sup>rd</sup> birthweight centile using centiles customised for ethnicity (GROW) compared to Intergrowth-21<sup>st</sup> birthweight centile (without such customisation), and only a small difference in specificity (93% versus 96%). The surrogate outcome of high dependency unit admission was used to assess severity of disease and women of Black ethnicity were significantly more likely to require this level of care after delivery (compared to White women), suggesting a correlation with increased disease severity amongst this group, and supported by a significantly higher proportion of preterm births that

were iatrogenic among mothers of Black ethnicity compared to White. This corresponds with the findings of another study that found an association between Black ethnicity and iatrogenic preterm delivery.<sup>31</sup>

### **Strengths and Limitations**

To our knowledge, this is the largest cohort study of women with chronic hypertension in pregnancy examining the impact of ethnicity on adverse perinatal outcome in the UK. The data were collated from three centres, which reduces the risk of confounding found in single-centre studies. Robust statistical methodology using regression modelling has allowed for identification and quantification of the impact of maternal factors on subsequent perinatal outcome.

The study has some limitations; it was not possible to assess the severity or duration of chronic hypertension within the cohort. Coding for superimposed pre-eclampsia was not sufficiently reliable given the complexities of this diagnosis in women with pre-existing hypertension<sup>20</sup> and so the additional impact of this diagnosis on adverse perinatal outcome could not be assessed. Additionally, adequately detailed data on blood pressure control, antihypertensive treatment, aspirin prescription, mode of conception and other maternal co-morbidity were not available. Comparison of temporal changes in care was not possible due to restrictions in the availability of this data; the only outcome that appeared to improve over time within the cohort was neonatal unit admission. Postcode data was utilised to assign socioeconomic status; this methodology may have led to incorrect attribution of level of deprivation, but as English postcode data relates to relatively small size areas compared to similar metrics in other countries, it is unlikely that use of this variable will have led to substantial inaccuracies. It is also likely that other characteristics included in the regression model will have allowed some adjustment for incorrect attribution of deprivation.

Although the cohort had free access to healthcare, it was not possible to assess adherence or uptake of antenatal care amongst differing ethnic groups. There may be cultural or language barriers that influence healthcare access, but the FASTER trial examined variation in perinatal outcomes in women who accessed antenatal care in the first trimester and found Black women had an increased risk of perinatal morbidity compared to White (OR 3.5; 95% CI 2.5 to 4.9), so this factor cannot entirely explain the difference in outcome.<sup>32</sup>

### Interpretation

Women of Black ethnicity with chronic hypertension are at significantly greater risk of all adverse perinatal outcomes than White women with chronic hypertension in pregnancy. Women of Asian and Other ethnicities are also at increased risk, but to a lesser extent. There are well described differences in pathophysiology causing hypertension that relate to ethnicity.<sup>8, 33</sup> Variation in socioeconomic circumstances have previously been linked to these differences,<sup>1</sup> but these cannot account entirely for the variances given that the model presented here included deprivation score as a baseline characteristic and the participants had free point-of-care access to a healthcare system for their antenatal care. Severity of maternal disease may also have contributed to these findings and highlights the need to optimise treatment strategies for these women. Outside pregnancy, national recommendations in the UK and US are that first-line antihypertensive agents are stratified based on ethnicity with Black women receiving calcium-channel blockers rather than angiotensin-converting enzyme inhibitors.<sup>19, 34</sup> Consideration of the potential role of first-line antihypertensive agent choice in women of African/Caribbean family origin, as is used outside pregnancy, is recommended, in order to evaluate whether this strategy might improve maternal and perinatal outcomes. Investigation of the impact of genetics in addition to environmental and cultural variations

may improve our understanding of why there is ethnic variation in outcome and how this might be ameliorated.

Comparison of customised and non-customised birthweight centiles has been discussed in recent studies in the general population.<sup>35, 36</sup> The importance of accounting for maternal ethnicity in the calculation of birthweight centiles is unclear. Ethnicity has a strong association with adverse outcome within this population of women with chronic hypertension and birthweight centiles customised for ethnicity have greater sensitivity and comparable specificity in association with an important outcome indicative of adverse perinatal outcome. Classification of fetal and hence neonatal growth restriction has recently been examined by a Delphi consensus outlining criteria for diagnosis of fetal growth restriction.<sup>26</sup> Further investigation into classification of neonatal growth restriction and the role of including ethnicity within birthweight centile calculation is warranted.<sup>26, 37</sup>

Non-White ethnicity (especially Black), deprivation, advanced maternal age, primiparity, and smoking status all increase the risk of adverse perinatal outcome in women with chronic hypertension. Ethnicity has the largest impact, with Black women with chronic hypertension at greatest risk. Further research is needed to explore the aetiology underpinning these disparities. An awareness of these differences should be considered to inform stratification of antenatal care and treatment pathways.



**ACKNOWLEDGEMENTS**

This is independent research supported by the National Institute for Health Research Professorship of Lucy Chappell RP-2014-05-019. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

**FUNDING**

This is independent research supported by the National Institute for Health Research Professorship of Lucy Chappell RP-2014-05-019. Paul Seed is funded by Tommy's Charity and the CLAHRC South London (NIHR). Dr Jenny Myers is supported by a NIHR Clinician Scientist Fellowship (NIHR-CS-011-020).

**CONFLICT OF INTEREST**

Professor Nelson-Piercy reports personal fees from Alliance Pharmaceuticals, UCB Pharmaceuticals, LEO Pharmaceuticals, Sanofi Aventis and Warner Chilcott outside the submitted work. The other investigators have no disclosures to report.

## REFERENCES

1. Tanaka M, Jaamaa G, Kaiser M, Hills E, Soim A, Zhu M, Shcherbatykh IY, Samelson R, Bell E, Zdeb M, McNutt LA. Racial disparity in hypertensive disorders of pregnancy in New York State: a 10-year longitudinal population-based study. *Am J Public Health*. 2007;97(1):163-70.
2. Bryant AS, Worjolah A, Caughey AB, Washington AE. Racial/ethnic disparities in obstetric outcomes and care: prevalence and determinants. *Am J Obstet Gynecol*. 2010;202(4):335-43.
3. Creanga AA, Berg CJ, Syverson C, Seed K, Bruce FC, Callaghan WM. Pregnancy-related mortality in the United States, 2006-2010. *Obstet Gynecol*. 2015 Jan;125(1):5-12.
4. Nair M, Kurinczuk JJ, Knight M. Ethnic variations in severe maternal morbidity in the UK—a case control study. *PLoS One*. 2014;9(4):e95086.
5. Bryant AS, Seely EW, Cohen A, Lieberman E. Patterns of pregnancy-related hypertension in black and white women. *Hypertens Pregnancy*. 2005;24(3):281-90.
6. Knight M, Kurinczuk JJ, Spark P, Brocklehurst P. Inequalities in maternal health: national cohort study of ethnic variation in severe maternal morbidities. *BMJ*. 2009;338:b542.
7. Harper M, Dugan E, Espeland M, Martinez-Borges A, McQuellon C. Why African-American women are at greater risk for pregnancy-related death. *Ann Epidemiol*. 2007;17(3):180-5.
8. Geronimus AT, Bound J, Keene D, Hicken M. Black-white differences in age trajectories of hypertension prevalence among adult women and men, 1999-2002. *Ethn Dis*. 2007;17(1):40-9.
9. Levine RS, Foster JE, Fullilove RE, Fullilove MT, Briggs NC, Hull PC, Husaini BA, Hennekens CH. Black-white inequalities in mortality and life expectancy, 1933–1999: implications for healthy people 2010. *Public Health Rep*. 2016.
10. Seely EW, Ecker J. Chronic hypertension in pregnancy. *Circulation*. 2014 Mar 18;129(11):1254-61.

11. Bateman BT, Bansil P, Hernandez-Diaz S, Mhyre JM, Callaghan WM, Kuklina EV. Prevalence, trends, and outcomes of chronic hypertension: a nationwide sample of delivery admissions. *Am J Obstet Gynecol*. 2012;206(2):134. e1-. e8.
12. Office of National Statistics. Statistical Bulletin Births in England and Wales, 2014. <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/bulletins/birthsummarytablesenglandandwales/2015-07-15>
13. Martin JA, Hamilton BE, Osterman M. Births in the United States, 2015. *NCHS Data Brief*. 2016;258:1-8.
14. Fisher S, Kim S, Sharma A, Rochat R, Morrow B. Is obesity still increasing among pregnant women? Prepregnancy obesity trends in 20 states, 2003–2009. *Prev Med*. 2013;56(6):372-8.
15. Bramham K, Parnell B, Nelson-Piercy C, Seed PT, Poston L, Chappell LC. Chronic hypertension and pregnancy outcomes: systematic review and meta-analysis. *BMJ*. 2014;348.
16. McCowan LM, Buist RG, North RA, Gamble G. Perinatal morbidity in chronic hypertension. *BJOG*. 1996;103(2):123-9.
17. Gilbert WM, Young AL, Danielsen B. Pregnancy outcomes in women with chronic hypertension: a population-based study. *J Reprod Med*. 2007;52(11):1046-51.
18. Allen VM, Joseph K, Murphy KE, Magee LA, Ohlsson A. The effect of hypertensive disorders in pregnancy on small for gestational age and stillbirth: a population based study. *BMC Pregnancy Childbirth*. 2004;4(1):17.
19. National Institute for Health and Clinical Excellence. Hypertension: Clinical management of primary hypertension in adults 2011. <https://www.nice.org.uk/Guidance/CG127>.
20. Tranquilli AL, Dekker G, Magee L, Roberts J, Sibai BM, Steyn W, Zeeman GG, Brown MA. The classification, diagnosis and management of the hypertensive disorders of pregnancy: a revised statement from the ISSHP. *Pregnancy Hypertens*. 2014;4(2):97-104.

21. Norwitz ER, Edusa V, Park JS. Maternal physiology and complications of multiple pregnancy. *Semin Perinatol*; 2005: Elsevier; 2005. p. 338-48.
22. Office for National Statistics. Ethnicity and National Identity in England and Wales: 2011.  
<http://www.ons.gov.uk/peoplepopulationandcommunity/culturalidentity/ethnicity/articles/ethnicityandnationalidentityinenglandandwales/2012-12-11>.
23. Department for Communities and Local Government. English indices of deprivation 2015. <https://www.gov.uk/government/statistics/english-indices-of-deprivation-2015>.
24. Gardosi J. New definition of small for gestational age based on fetal growth potential. *Horm Res Paediatr*. 2006;65(Suppl. 3):15-8.
25. Villar J, Ismail LC, Victora CG, Ohuma EO, Bertino E, Altman DG, Lambert A, Papageorghiou AT, Carvalho M, Jaffer YA, Gravett MG. International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21 st Project. *The Lancet*. 2014;384(9946):857-68.
26. Gordijn SJ, Beune IM, Thilaganathan B, Papageorghiou A, Baschat AA, Baker PN, Silver RM, Wynia K, Ganzevoort W. Consensus definition of fetal growth restriction: a Delphi procedure. *Ultrasound Obstet Gynecol*. 2016 Sep;48(3):333-9.
27. PLOS Medicine Editors. Observational studies: getting clear about transparency. *PLoS med*. 2014 Aug 26;11(8):e1001711.
28. Kenny LC, Lavender T, McNamee R, O'Neill SM, Mills T, Khashan AS. Advanced maternal age and adverse pregnancy outcome: evidence from a large contemporary cohort. *PLoS One*. 2013;8(2):e56583.
29. Castles A, Adams EK, Melvin CL, Kelsch C, Boulton ML. Effects of smoking during pregnancy: five meta-analyses. *Am J Prev Med*. 1999;16(3):208-15.

30. Office of National Statistics. Childhood mortality in England and Wales.  
<https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/childhoodinfantandperinatalmortalityinenglandandwales/2014>.
31. Premkumar A, Henry DE, Moghadassi M, Nakagawa S, Norton ME. The interaction between maternal race/ethnicity and chronic hypertension on preterm birth. *Am J Obstet Gynecol*. 2016;215(6):787. e1-. e8.
32. Healy AJ, Malone FD, Sullivan LM, Porter TF, Luthy DA, Comstock CH, Saade G, Berkowitz R, Klugman S, Dugoff L, Craigo SD. Early access to prenatal care: implications for racial disparity in perinatal mortality. *Obstet Gynecol*. 2006;107(3):625-31.
33. Gillum RF. Epidemiology of hypertension in African American women. *Am Heart J*. 1996;131(2):385-95.
34. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, Lackland DT, LeFevre ML, MacKenzie TD, Ogedegbe O, Smith SC. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311(5):507-20.
35. Iliodromiti S, Mackay DF, Smith GC, Pell JP, Sattar N, Lawlor DA, Nelson SM. Customised and Noncustomised Birth Weight Centiles and Prediction of Stillbirth and Infant Mortality and Morbidity: A Cohort Study of 979,912 Term Singleton Pregnancies in Scotland. *PLoS Med*. 2017;14(1):e1002228.
36. Louis GM, Grewal J, Albert PS, Sciscione A, Wing DA, Grobman WA, Newman RB, Wapner R, D'alton ME, Skupski D, Nageotte MP. Racial/ethnic standards for fetal growth: the NICHD Fetal Growth Studies. *Am J Obstet Gynecol*. 2015;213(4):449-e1.
37. Stock SJ, Myers J. Defining Abnormal Fetal Growth and Perinatal Risk: Population or Customized Standards? *PLoS Med*. 2017;14(1):e1002229.

## FIGURE LEGENDS

**Figure 1:** Flow diagram of identification of the study cohort

## TABLES

**Table 1:** Demographic characteristics of the whole cohort with chronic hypertension and by ethnic group

<b>Maternal Characteristic</b>	<b>All pregnancies n=4481</b>	<b>White ethnicity n=2122</b>	<b>Black ethnicity n=1601</b>	<b>Asian ethnicity n=379</b>
<b>Age at delivery, years mean (SD)</b>	33 (5.8)	33 (5.5)	34 (6.2)	32 (5.3)
<b>Body Mass Index, kg/m<sup>2</sup> mean (SD)</b>	28 (6.4)	27 (6.4)	30 (6.3)	28 (5.2)
<b>Nulliparous</b>	2112 (47%)	1210 (57%)	553 (35%)	135 (36%)
<b>Smoker</b>	312 (7%)	209 (9.9%)	71 (4.4%)	11 (2.9%)
<b>Deprivation Index</b>				
1 (least deprived)	350 (8%)	288 (14%)	21 (1.3%)	19 (5.0%)
2	462 (10%)	339 (16%)	54 (3.4%)	36 (9.5%)
3	953 (21%)	522 (25%)	242 (15%)	98 (26%)
4	1403 (32%)	575 (27%)	574 (36%)	123 (32%)
5 (most deprived)	1313 (29%)	398 (19%)	710 (44%)	103 (27%)
<b>Year of pregnancy</b>				
2000-2004	836 (19%)	404 (19%)	318 (20%)	60 (16%)
2005-2009	1598 (36%)	770 (36%)	575 (36%)	128 (34%)
2010-2014	2047 (45%)	948 (45%)	708 (44%)	191 (50%)

*SD= standard deviation*

**Table 2:** Maternal and perinatal outcomes of the whole cohort with chronic hypertension and by ethnic group

	All pregnancies n=4481	White ethnicity n=2122	Black ethnicity n=1601	Asian ethnicity n=379
<b>Maternal Outcomes</b>				
<b>Gestation at delivery, weeks</b>	39.3	39.7	39.0	39.0
<b>median (IQR)</b>	(38.0 to 40.4)	(38.3 to 40.7)	(37.4 to 40.1)	(37.0 to 40.0)
<b>Onset of labour</b>				
Spontaneous	1832 (41%)	942 (45%)	558 (35%)	154 (41%)
Induction	1471 (33%)	709 (34%)	542 (34%)	91 (24%)
Pre-labour caesarean section	1007 (23%)	329 (16%)	399 (25%)	101 (27%)
<b>Mode of delivery</b>				
Unassisted vaginal delivery	2152 (48%)	1039 (49%)	758 (47%)	180 (47%)
Assisted vaginal delivery	580 (13%)	376 (18%)	113 (7.1%)	39 (10%)
Caesarean section delivery	1749 (39%)	706 (33%)	727 (45%)	160 (42%)
<b>High dependency unit admission</b>	417 (11%)	151 (7.1%)	201 (13%)	26 (6.9%)
<b>Fetal outcomes</b>				
<b>Stillbirth</b>	72 (1.6%)	12 (0.6%)	49 (3.1%)	6 (1.6%)
<b>Preterm birth</b>				
<37 weeks	701 (16%)	236 (11%)	335 (21%)	77 (20%)
<34 weeks	305 (6.8%)	76 (3.6%)	170 (11%)	35 (9.2%)
<b>Birthweight, g,</b>	3230	3350	3100	3000
<b>median (IQR)</b>	(2780 to 3630)	(2960 to 3740)	(2560 to 3520)	(2600 to 3380)
<b>Birthweight centile (GROW)</b>				
<10 <sup>th</sup> centile	1047 (23%)	389 (18%)	492 (31%)	82 (22%)
<3 <sup>rd</sup> centile	499 (11%)	157 (7.4%)	248 (15%)	46 (12%)
<b>Neonatal unit admission</b>	413 (9.2%)	156 (7.4%)	176 (11%)	40 (11%)

*IQR= interquartile range*



**Table 3:** Adjusted risk ratios (95% confidence intervals) of significant maternal characteristics

associated with adverse perinatal outcomes in women with chronic hypertension

Perinatal outcome	Black versus White women	Asian versus White women	Maternal age >40 years versus <25 years	Smokers versus non-smokers	Primip versus multip	Deprivation Index group 5* versus 1 to 3
Stillbirth	<b>5.56</b> (2.79 to 11.09)	<b>3.03</b> (1.11 to 8.28)	1.07 (0.54 to 2.13)	0.53 (0.12 to 2.20)	1.56 (0.94 to 2.60)	1.31 (0.60 to 2.12)
Birthweight <10 <sup>th</sup> centile	<b>1.64</b> (1.45 to 1.87)	1.21 (0.97 to 1.51)	<b>1.34</b> (1.06 to 1.69)	<b>1.52</b> (1.28 to 1.81)	<b>1.16</b> (1.03 to 1.30)	<b>1.20</b> (1.04 to 1.38)
Birthweight <3 <sup>rd</sup> centile	<b>2.07</b> (1.71 to 2.51)	<b>1.69</b> (1.24 to 2.30)	<b>1.53</b> (1.09 to 2.16)	<b>1.53</b> (1.15 to 2.04)	1.19 (0.99 to 1.42)	1.14 (0.92 to 1.42)
Preterm <37 weeks	<b>1.70</b> (1.43 to 2.01)	<b>1.82</b> (1.41 to 2.35)	<b>1.52</b> (1.13 to 2.05)	1.26 (0.97 to 1.63)	<b>1.17</b> (1.01 to 1.35)	<b>1.42</b> (1.18 to 1.70)
Preterm <34 weeks	<b>2.69</b> (2.03 to 3.55)	<b>2.48</b> (1.69 to 3.66)	1.39 (0.99 to 1.94)	1.34 (0.87 to 2.07)	1.18 (0.94 to 1.49)	<b>1.39</b> (1.05 to 1.86)
Neonatal unit admission	<b>1.55</b> (1.25 to 1.93)	<b>1.58</b> (1.12 to 2.23)	1.38 (0.93 to 2.04)	1.29 (0.92 to 1.82)	<b>1.32</b> (1.08 to 1.61)	1.12 (0.88 to 1.43)

\*Deprivation index group 5 is associated with the greatest deprivation. Significant risk ratios

are in bold type.

